

REMARKS

Upon entry of this Amendment and Response claims 4 and 6-18 will be pending in this application. Claims 1-3 have been cancelled without prejudice. Claims 4, 6, 7, 11-13, 16 and 17 have been amended. Reconsideration is respectfully requested.

**I. Rejection Under 35 U.S.C. §112**

Claims 1-4, 6-16, 17 and 18 have been rejected as allegedly being nonenabling and indefinite. In particular, the Office Action states that use of the term “derivatives” renders the claim indefinite and fails to define the scope of the claim.

Claims 1-3 have been cancelled and other claims having the term “derivatives” have been amended to incorporate a specific compound structure thereby obviating these rejections.

Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112.

**II. Rejection Under 35 U.S.C. §103(a)**

Claims 1-4, 6-13 and 16 have been rejected under 35 U.S.C. §103(a) as allegedly being obvious over JP 02262519 (“JP ‘519”) in view of Monaghan *et al.* (PCT Publication No. WO 98/57972). In particular, the Office Action alleges motivation to combine the teachings of JP ‘519 with Monaghan *et al.* resides in the fact that both are directed towards treating nerve diseases associated with diabetes.

JP ‘519 merely discusses that Beraprost is effective for treatment of diabetic neuropathy. In particular, JP ‘519 teaches that the ammonium salt of Beraprost can improve the solubility of Beraprost as a result of forming an ammonium salt, but it is silent as to whether this salt can increase the oil/water partition coefficient or whether such a mixture exhibits a sustained-release activity.

Monaghan *et al.* discuss tachykinin antagonists which are a salt of a tachykinin compound containing a quaternary ammonium moiety in the molecular structure thereof with an anion as an opposite electron charge, such as chlorine ion or methanesulfonic ion. Monaghan *et al.* teach the molecular modification of the tachykinin antagonists for the alteration of the physical property of the active ingredient, e.g., tachykinin antagonist. Monaghan *et al.* discuss that such salts are also effective against diabetic neuropathy. Monaghan *et al.* also discuss that this type of salt can improve the solubility. However, similar to JP '519, Monaghan *et al.* are silent as to whether this salt can increase the oil/water partition coefficient or a sustained-release activity. Therefore, Monaghan *et al.* do not make-up the deficiencies in JP '519.

In contrast, compositions of the present invention provide an increased oil/water partition coefficient and allow sustained-release of the compound of Formula I (see Claim 4, hereinafter referred to as "metaphenylene compound"). These properties are achieved by combining the compound of Formula I (i.e., metaphenylene compound) with an ionic compound having an opposite electron charge that are capable of increasing the oil/water partition coefficient. Suitable ionic compounds can be readily identified by one skilled in the art by simply testing its effect on the oil/water partition coefficient of the metaphenylene compound.

Furthermore, compositions of the present invention are directed to a sustained-release composition. As set forth on page 6, lines 7-15 of the English translated specification, the pharmaceutical compositions of the present invention are far superior to the prostanoic acid derivatives alone because, *inter alia*, of increased partition coefficients and sustained-release effects. Moreover, sustained-release compositions of the present invention reduce the number of treatment and/or application needed as well as the application doses. In addition, sustained-release compositions of the present invention may reduce the side effects.

As will be recognized, claims cannot be found obvious unless the prior art **teaches or suggests** making the claimed product. *See In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) (The teaching or suggestion to make the claimed combination or

modification and the reasonable expectation of success must **both be found** in the prior art), *In re Mills*, 16 USPQ2d 1430 (Fed. Cir., 1990) (The mere fact that references can be combined or modified does **not** render the resultant combination or modification obvious **unless** the prior art also **suggests the desirability** of the combination or modification.) There must be something in the prior art that would have motivated persons of ordinary skill to make the combination. *In re Stencel*, 4 U.S.P.Q.2d 1071, 1073 (Fed. Cir. 1987), *accord*, *Ex parte Marinaccio*, 10 U.S.P.Q.2d 1716 (Pat. Off. Bd. App. 1989) (combining references is improper absent some teaching, suggestion, or motivation for the combination in the prior art), *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990) (The mere fact that references can be combined or modified does **not** render the resultant combination or modification obvious **unless** the prior art also **suggests the desirability** of the combination or modification. Thus, although a prior art device “may be capable of being modified to run the way the apparatus is claimed, there **must be a suggestion or motivation in the reference** to do so”).

Neither the JP ‘519 nor Monaghan *et al.* teach or suggest a sustained-release composition or a composition having an increased oil/water partition coefficient. Therefore, the rejection under 35 U.S.C. §103(a) is improper.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

#### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

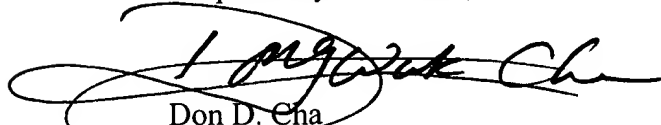
If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

PATENT

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Respectfully submitted,



Don D. Cha  
Reg. No. 40,945

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: 925-472-5000  
Fax: 415-576-0300  
DDC:ddc

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